

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: GARABEDIAN=2A

In re Application of:)	Art Unit: 1647
)	
Michael GARABEDIAN)	Examiner: Daniel C. Gamett
)	
Appln. No.: 10/629,913)	Washington, D.C.
)	
Date Filed: July 30, 2003)	Confirmation No. 8615
)	
For: ANTIBODIES THAT RECOGNIZE)	
AND BIND PHOSPHORYLATED...)	

DECLARATION UNDER 37 CFR §1.132

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
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Sir:

We, Michael Garabedian and Zhen Wang, hereby declare
and state as follows:

We are the same Michael Garabedian and Zhen Wang who
are the co-inventors of the invention(s) disclosed and claimed
in the above-identified application no. 10/629,913.

We are also the same Michael Garabedian and Zhen
Wang who are listed among the co-authors of the publication,
Wang, Z., Frederick, J. and Garabedian, M. "Deciphering the
Phosphorylation 'Code' of the Glucocorticoid Receptor *In Vivo*"
J. Biol. Chem. 277(29):26573-26580 (2002).

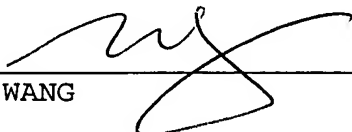
Also listed as co-author on the above publication was Jeremy Frederick. While Jeremy Frederick was a co-author and a co-worker with us, he was not involved in the conception and is not a co-inventor of the invention(s) claimed in the above-identified application no. 10/629,913.



The undersigned declare further that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

4/21/05
Date


Michael GARABEDIAN

4/20/2005
Date


Zhen WANG

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☐ 1: [P04150](#). Reports Glucocorticoid re...[gi:121069]
 BLink, Domains, Links

LOCUS P04150 777 aa linear PRI 01-MAY-2005
 DEFINITION Glucocorticoid receptor (GR).
 ACCESSION P04150
 VERSION P04150 GI:121069
 DBSOURCE swissprot: locus GCR_HUMAN, accession [P04150](#);
 class: standard.
 extra accessions: P04151, created: Nov 1, 1986.
 sequence updated: Nov 1, 1986.
 annotation updated: May 1, 2005.
 xrefs: [X03225.1](#), [CAA26976.1](#), [X03348.1](#), [CAA27054.1](#), [U80946.1](#),
[AAB64353.1](#), [U78506.1](#), [U78507.1](#), [U78508.1](#), [U78509.1](#), [U78510.1](#),
[U78511.1](#), [U78512.1](#), [U80947.1](#), [AAB64354.1](#), [U01351.1](#), [AAA16603.1](#),
[AY436590.1](#), [AAQ97180.1](#), [BC015610.2](#), [AAH15610.1](#), [M69104.1](#),
[AAA88049.1](#), [M73816.1](#), [AAA53151.1](#), [S68378.1](#), [AAB20466.1](#), [AC005601.1](#),
[AAC34207.1](#), [QRHUGA](#), [QRHUGB](#), [1M2ZA](#), [1M2ZD](#), [1NHZA](#), [1P93A](#), [1P93B](#),
[1P93C](#), [1P93D](#)
 xrefs (non-sequence databases): [SMRP04150](#), [IntActP04150](#),
[TRANSFACT00337](#), [TRANSFACT01920](#), [EnsemblENSG00000113580](#),
[GenewHGNC:7978](#), [H-InvDBHIX0005273](#), [MIM 138040](#), [GO0005737](#),
[GO0005759](#), [GO0005634](#), [GO0004883](#), [GO0003700](#), [GO0007165](#), [GO0006366](#),
[InterProIPR001409](#), [InterProIPR000536](#), [InterProIPR001723](#),
[InterProIPR008946](#), [InterProIPR001628](#), [PfamPF02155](#), [PfamPF00104](#),
[PfamPF00105](#), [PRINTSPR00528](#), [PRINTSPR00398](#), [PRINTSPR00047](#),
[ProDomPD000035](#), [SMARTSM00430](#), [SMARTSM00399](#), [PROSITEPS00031](#),
[PROSITEPS51030](#)
 KEYWORDS 3D-structure; Alternative initiation; Alternative splicing; Disease
 mutation; DNA-binding; Metal-binding; Nuclear protein;
 Phosphorylation; Polymorphism; Receptor; Steroid-binding;
 Trans-acting factor; Transcription; Transcription regulation; Ubl
 conjugation; Zinc; Zinc-finger.
 SOURCE Homo sapiens (human)
 ORGANISM [Homo sapiens](#)
[Eukaryota](#); [Metazoa](#); [Chordata](#); [Craniata](#); [Vertebrata](#); [Euteleostomi](#);
[Mammalia](#); [Eutheria](#); [Euarchontoglires](#); [Primates](#); [Catarrhini](#);
[Hominidae](#); [Homo](#).
 REFERENCE 1 (residues 1 to 777)
 AUTHORS Hollenberg,S.M., Weinberger,C., Ong,E.S., Cerelli,G., Oro,A.,
 Lebo,R., Thompson,E.B., Rosenfeld,M.G. and Evans,R.M.
 TITLE Primary structure and expression of a functional human
 glucocorticoid receptor cDNA
 JOURNAL Nature 318 (6047), 635-641 (1985)
 PUBMED 2867473
 REMARK NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS ALPHA AND BETA).
 TISSUE=Fibroblast
 REFERENCE 2 (residues 1 to 777)
 AUTHORS Encio,I.J. and Detera-Wadleigh,S.D.
 TITLE The genomic structure of the human glucocorticoid receptor
 JOURNAL J. Biol. Chem. 266 (11), 7182-7188 (1991)

PUBMED 1707881
 REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORMS ALPHA AND BETA).
 REFERENCE 3 (residues 1 to 777)
 AUTHORS Munroe,D.G., Pang,J., Taylor,G.R., Lau,C., Plante,R.K. and Zhou,L.
 TITLE Direct Submission
 JOURNAL Submitted (??-SEP-1993)
 REMARK NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM GAMMA).
 REFERENCE 4 (residues 1 to 777)
 AUTHORS Rieder,M.J., Livingston,R.J., Daniels,M.R., Chung,M.-W.,
 Miyamoto,K.E., Nguyen,C.P., Nguyen,D.A., Poel,C.L., Robertson,P.D.,
 Schackwitz,W.S., Sherwood,J.K., Witrak,L.A. and Nickerson,D.A.
 TITLE Direct Submission
 JOURNAL Submitted (??-OCT-2003)
 REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM ALPHA), AND VARIANTS
 LYS-23 AND VAL-65.
 REFERENCE 5 (residues 1 to 777)
 AUTHORS Strausberg,R.L., Feingold,E.A., Grouse,L.H., Derge,J.G.,
 Klausner,R.D., Collins,F.S., Wagner,L., Shenmen,C.M., Schuler,G.D.,
 Altschul,S.F., Zeeberg,B., Buetow,K.H., Schaefer,C.F., Bhat,N.K.,
 Hopkins,R.F., Jordan,H., Moore,T., Max,S.I., Wang,J., Hsieh,F.,
 Diatchenko,L., Marusina,K., Farmer,A.A., Rubin,G.M., Hong,L.,
 Stapleton,M., Soares,M.B., Bonaldo,M.F., Casavant,T.L.,
 Scheetz,T.E., Brownstein,M.J., Usdin,T.B., Toshiyuki,S.,
 Carninci,P., Prange,C., Raha,S.S., Loquellano,N.A., Peters,G.J.,
 Abramson,R.D., Mullahy,S.J., Bosak,S.A., McEwan,P.J.,
 McKernan,K.J., Malek,J.A., Gunaratne,P.H., Richards,S.,
 Worley,K.C., Hale,S., Garcia,A.M., Gay,L.J., Hulyk,S.W.,
 Villalón,D.K., Muzny,D.M., Sodergren,E.J., Lu,X., Gibbs,R.A.,
 Fahey,J., Helton,E., Kettelman,M., Madan,A., Rodrigues,S.,
 Sanchez,A., Whiting,M., Madan,A., Young,A.C., Shevchenko,Y.,
 Bouffard,G.G., Blakesley,R.W., Touchman,J.W., Green,E.D.,
 Dickson,M.C., Rodriguez,A.C., Grimwood,J., Schmutz,J., Myers,R.M.,
 Butterfield,Y.S., Krzywinski,M.I., Skalska,U., Smailus,D.E.,
 Schnerch,A., Schein,J.E., Jones,S.J. and Marra,M.A.
 CONSRTM Mammalian Gene Collection Program Team
 TITLE Generation and initial analysis of more than 15,000 full-length
 human and mouse cDNA sequences
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)
 PUBMED 12477932
 REMARK NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM ALPHA).
 TISSUE=Placenta
 REFERENCE 6 (residues 1 to 777)
 AUTHORS Leclerc,S., Xie,B.X., Roy,R. and Govindan,M.V.
 TITLE Purification of a human glucocorticoid receptor gene
 promoter-binding protein. Production of polyclonal antibodies
 against the purified factor
 JOURNAL J. Biol. Chem. 266 (14), 8711-8719 (1991)
 PUBMED 2026589
 REMARK NUCLEOTIDE SEQUENCE OF 1-394.
 REFERENCE 7 (residues 1 to 777)
 AUTHORS Govindan,M.V., Pothier,F., Leclerc,S., Palaniswami,R. and Xie,B.
 TITLE Human glucocorticoid receptor gene promoter-homologous down
 regulation
 JOURNAL J. Steroid Biochem. Mol. Biol. 40 (1-3), 317-323 (1991)
 PUBMED 1958537
 REMARK NUCLEOTIDE SEQUENCE OF 1-394.
 REFERENCE 8 (residues 1 to 777)
 AUTHORS Kimmerly,W., Bondoc,M., Cheng,J., Connolly,K.S., Gunning,K.M.,
 Kadner,K., Miguel,T., Miller,C., Pitluck,S., Pollard,M.,
 Rojeski,H., Subramanian,S. and Martin,C.H.
 TITLE Direct Submission
 JOURNAL Submitted (??-SEP-1998)
 REMARK NUCLEOTIDE SEQUENCE OF 396-630.
 REFERENCE 9 (residues 1 to 777)
 AUTHORS Yudit,M.R. and Cidlowski,J.A.
 TITLE Molecular identification and characterization of a and b forms of
 the glucocorticoid receptor

JOURNAL Mol. Endocrinol. 15 (7), 1093-1103 (2001)
PUBMED 11435610
REMARK ALTERNATIVE INITIATION, AND MUTAGENESIS OF MET-1 AND MET-27.
REFERENCE 10 (residues 1 to 777)
AUTHORS Weinberger,C., Hollenberg,S.M., Rosenfeld,M.G. and Evans,R.M.
TITLE Domain structure of human glucocorticoid receptor and its
relationship to the v-erb-A oncogene product
JOURNAL Nature 318 (6047), 670-672 (1985)
PUBMED 3841189
REMARK DOMAINS.
REFERENCE 11 (residues 1 to 777)
AUTHORS Henriksson,A., Almlof,T., Ford,J., McEwan,I.J., Gustafsson,J.A. and
Wright,A.P.
TITLE Role of the Ada adaptor complex in gene activation by the
glucocorticoid receptor
JOURNAL Mol. Cell. Biol. 17 (6), 3065-3073 (1997)
PUBMED 9154805
REMARK INTERACTIONS WITH TADA2L AND THE ADA COMPLEX, AND MUTAGENESIS OF
PHE-191; ILE-193; LEU-194; LEU-197; TRP-213; LEU-224; LEU-225;
PHE-235 AND LEU-236.
REFERENCE 12 (residues 1 to 777)
AUTHORS Fryer,C.J. and Archer,T.K.
TITLE Chromatin remodelling by the glucocorticoid receptor requires the
BRG1 complex
JOURNAL Nature 393 (6680), 88-91 (1998)
PUBMED 9590696
REMARK INTERACTIONS WITH THE SMARCA4 COMPLEX; NCOA1; NCOA2 AND THE
CREBBP/EP300 COMPLEX.
REFERENCE 13 (residues 1 to 777)
AUTHORS Schneikert,J., Hubner,S., Martin,E. and Cato,A.C.
TITLE A nuclear action of the eukaryotic cochaperone RAP46 in
downregulation of glucocorticoid receptor activity
JOURNAL J. Cell Biol. 146 (5), 929-940 (1999)
PUBMED 10477749
REMARK INTERACTION WITH BAG1.
REFERENCE 14 (residues 1 to 777)
AUTHORS Rivers,C., Levy,A., Hancock,J., Lightman,S. and Norman,M.
TITLE Insertion of an amino acid in the DNA-binding domain of the
glucocorticoid receptor as a result of alternative splicing
JOURNAL J. Clin. Endocrinol. Metab. 84 (11), 4283-4286 (1999)
PUBMED 10566686
REMARK ALTERNATIVE SPLICING (ISOFORM GAMMA).
REFERENCE 15 (residues 1 to 777)
AUTHORS Moalli,P.A., Pillay,S., Krett,N.L. and Rosen,S.T.
TITLE Alternatively spliced glucocorticoid receptor messenger RNAs in
glucocorticoid-resistant human multiple myeloma cells
JOURNAL Cancer Res. 53 (17), 3877-3879 (1993)
PUBMED 8358712
REMARK ALTERNATIVE SPLICING (ISOFORMS GP-P AND GP-A).
REFERENCE 16 (residues 1 to 777)
AUTHORS Lu,N.Z. and Cidlowski,J.A.
TITLE The origin and functions of multiple human glucocorticoid receptor
isoforms
JOURNAL Ann. N. Y. Acad. Sci. 1024, 102-123 (2004)
PUBMED 15265776
REMARK REVIEW ON ALTERNATIVE SPLICING, ALTERNATIVE INITIATION, AND
POSTTRANSLATIONAL MODIFICATIONS.
REFERENCE 17 (residues 1 to 777)
AUTHORS Mahajan,M.A. and Samuels,H.H.
TITLE A new family of nuclear receptor coregulators that integrate
nuclear receptor signaling through CREB-binding protein
JOURNAL Mol. Cell. Biol. 20 (14), 5048-5063 (2000)
PUBMED 10866662
REMARK INTERACTION WITH NCOA6.
REFERENCE 18 (residues 1 to 777)
AUTHORS Wallace,A.D. and Cidlowski,J.A.
TITLE Proteasome-mediated glucocorticoid receptor degradation restricts

transcriptional signaling by glucocorticoids

JOURNAL J. Biol. Chem. 276 (46), 42714-42721 (2001)

PUBMED 11555652

REMARK GLUCOCORTICOID-MEDIATED DOWN-REGULATION.

REFERENCE 19 (residues 1 to 777)

AUTHORS Tian,S., Poukka,H., Palvimo,J.J. and Janne,O.A.

TITLE Small ubiquitin-related modifier-1 (SUMO-1) modification of the glucocorticoid receptor

JOURNAL Biochem. J. 367 (PT 3), 907-911 (2002)

PUBMED 12144530

REMARK SUMOYLATION, AND MUTAGENESIS OF LYS-277; LYS-293 AND LYS-703.

REFERENCE 20 (residues 1 to 777)

AUTHORS Wang,Z., Frederick,J. and Garabedian,M.J.

TITLE Deciphering the phosphorylation 'code' of the glucocorticoid receptor in vivo

JOURNAL J. Biol. Chem. 277 (29), 26573-26580 (2002)

PUBMED 12000743

REMARK PHOSPHORYLATION SITES SER-203 AND SER-211.

REFERENCE 21 (residues 1 to 777)

AUTHORS Bledsoe,R.K., Montana,V.G., Stanley,T.B., Delves,C.J., Apolito,C.J., McKee,D.D., Consler,T.G., Parks,D.J., Stewart,E.L., Willson,T.M., Lambert,M.H., Moore,J.T., Pearce,K.H. and Xu,H.E.

TITLE Crystal structure of the glucocorticoid receptor ligand binding domain reveals a novel mode of receptor dimerization and coactivator recognition

JOURNAL Cell 110 (1), 93-105 (2002)

PUBMED 12151000

REMARK X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS) OF 521-777 OF MUTANT SER-602 IN COMPLEX WITH NCOA2; DEXAMETHASONE AND RU-486, AND MUTAGENESIS OF ARG-585; ASP-590; PHE-602; PRO-625 AND ILE-628.

REFERENCE 22 (residues 1 to 777)

AUTHORS Kauppi,B., Jakob,C., Farnegardh,M., Yang,J., Ahola,H., Alarcon,M., Calles,K., Engstrom,O., Harlan,J., Muchmore,S., Ramqvist,A.K., Thorell,S., Ohman,L., Greer,J., Gustafsson,J.A., Carlstedt-Duke,J. and Carlquist,M.

TITLE The three-dimensional structures of antagonistic and agonistic forms of the glucocorticoid receptor ligand-binding domain: RU-486 induces a transconformation that leads to active antagonism

JOURNAL J. Biol. Chem. 278 (25), 22748-22754 (2003)

PUBMED 12686538

REMARK X-RAY CRYSTALLOGRAPHY (2.3 ANGSTROMS) OF 500-777 OF MUTANT SER-602 IN COMPLEX WITH COACTIVATOR PEPTIDE; DEXAMETHASONE AND WITH RU-486.

REFERENCE 23 (residues 1 to 777)

AUTHORS Hurley,D.M., Accili,D., Stratakis,C.A., Karl,M., Vamvakopoulos,N., Rorer,E., Constantine,K., Taylor,S.I. and Chrousos,G.P.

TITLE Point mutation causing a single amino acid substitution in the hormone binding domain of the glucocorticoid receptor in familial glucocorticoid resistance

JOURNAL J. Clin. Invest. 87 (2), 680-686 (1991)

PUBMED 1704018

REMARK CHARACTERIZATION OF VARIANT GLUCOCORTICOID RESISTANCE VAL-641.

REFERENCE 24 (residues 1 to 777)

AUTHORS Powers,J.H., Hillmann,A.G., Tang,D.C. and Harmon,J.M.

TITLE Cloning and expression of mutant glucocorticoid receptors from glucocorticoid-sensitive and -resistant human leukemic cells

JOURNAL Cancer Res. 53 (17), 4059-4065 (1993)

PUBMED 8358735

REMARK VARIANTS TYR-421 AND PHE-753.

REFERENCE 25 (residues 1 to 777)

AUTHORS Karl,M., Lamberts,S.W., Detera-Wadleigh,S.D., Encio,I.J., Stratakis,C.A., Hurley,D.M., Accili,D. and Chrousos,G.P.

TITLE Familial glucocorticoid resistance caused by a splice site deletion in the human glucocorticoid receptor gene

JOURNAL J. Clin. Endocrinol. Metab. 76 (3), 683-689 (1993)

PUBMED 8445027

REMARK VARIANT SER-363.

REFERENCE 26 (residues 1 to 777)

AUTHORS Malchoff,D.M., Brufsky,A., Reardon,G., McDermott,P., Javier,E.C., Bergh,C.H., Rowe,D. and Malchoff,C.D.

TITLE A mutation of the glucocorticoid receptor in primary cortisol resistance

JOURNAL J. Clin. Invest. 91 (5), 1918-1925 (1993)

PUBMED 7683692

REMARK VARIANT GLUCOCORTICOID RESISTANCE ILE-729.

REFERENCE 27 (residues 1 to 777)

AUTHORS Ashraf,J. and Thompson,E.B.

TITLE Identification of the activation-labile gene: a single point mutation in the human glucocorticoid receptor presents as two distinct receptor phenotypes

JOURNAL Mol. Endocrinol. 7 (5), 631-642 (1993)

PUBMED 8316249

REMARK VARIANT PHE-753.

REFERENCE 28 (residues 1 to 777)

AUTHORS Koper,J.W., Stolk,R.P., de Lange,P., Huizenga,N.A.T.M., Molijn,G.-J., Pols,H.A.P., Grobbee,D.E., Karl,M., de Jong,F.H., Brinkmann,A.O. and Lamberts,S.W.J.

TITLE Lack of association between five polymorphisms in the human glucocorticoid receptor gene and glucocorticoid resistance

JOURNAL Hum. Genet. 99 (5), 663-668 (1997)

PUBMED 9150737

REMARK VARIANTS LYS-23 AND SER-363.

REFERENCE 29 (residues 1 to 777)

AUTHORS Cargill,M., Altshuler,D., Ireland,J., Sklar,P., Ardlie,K., Patil,N., Shaw,N., Lane,C.R., Lim,E.P., Kalyanaraman,N., Nemesh,J., Ziaugra,L., Friedland,L., Rolfe,A., Warrington,J., Lipshutz,R., Daley,G.Q. and Lander,E.S.

TITLE Characterization of single-nucleotide polymorphisms in coding regions of human genes

JOURNAL Nat. Genet. 22 (3), 231-238 (1999)

PUBMED 10391209

REMARK VARIANTS LYS-23; VAL-65 AND SER-363.

REFERENCE 30 (residues 1 to 777)

AUTHORS Cargill,M., Altshuler,D., Ireland,J., Sklar,P., Ardlie,K., Patil,N., Shaw,N., Lane,C.R., Lim,E.P., Kalyanaraman,N., Nemesh,J., Ziaugra,L., Friedland,L., Rolfe,A., Warrington,J., Lipshutz,R., Daley,G.Q. and Lander,E.S.

JOURNAL Nat. Genet. 23, 373-373 (1999)

REMARK ERRATUM.

REFERENCE 31 (residues 1 to 777)

AUTHORS Feng,J., Zheng,J., Bennett,W.P., Heston,L.L., Jones,I.R., Craddock,N. and Sommer,S.S.

TITLE Five missense variants in the amino-terminal domain of the glucocorticoid receptor: no association with puerperal psychosis or schizophrenia

JOURNAL Am. J. Med. Genet. 96 (3), 412-417 (2000)

PUBMED 10898924

REMARK VARIANTS LYS-23; LEU-29; PHE-112; ASN-233 AND SER-363.

REFERENCE 32 (residues 1 to 777)

AUTHORS Ruiz,M., Lind,U., Gafvels,M., Eggertsen,G., Carlstedt-Duke,J., Nilsson,L., Holtmann,M., Stierna,P., Wikstrom,A.C. and Werner,S.

TITLE Characterization of two novel mutations in the glucocorticoid receptor gene in patients with primary cortisol resistance

JOURNAL Clin. Endocrinol. (Oxf) 55 (3), 363-371 (2001)

PUBMED 11589680

REMARK VARIANTS GLUCOCORTICOID RESISTANCE HIS-477 AND SER-679.

REFERENCE 33 (residues 1 to 777)

AUTHORS Kino,T., Stauber,R.H., Resau,J.H., Pavlakis,G.N. and Chrousos,G.P.

TITLE Pathologic human GR mutant has a transdominant negative effect on the wild-type GR by inhibiting its translocation into the nucleus: importance of the ligand-binding domain for intracellular GR trafficking

JOURNAL J. Clin. Endocrinol. Metab. 86 (11), 5600-5608 (2001)

PUBMED 11701741

REMARK CHARACTERIZATION OF VARIANT GLUCOCORTICOID RESISTANCE ASN-559.

REFERENCE 34 (residues 1 to 777)

AUTHORS Vottero,A., Kino,T., Combe,H., Lecomte,P. and Chrousos,G.P.

TITLE A novel, C-terminal dominant negative mutation of the GR causes familial glucocorticoid resistance through abnormal interactions with p160 steroid receptor coactivators

JOURNAL J. Clin. Endocrinol. Metab. 87 (6), 2658-2667 (2002)

PUBMED 12050230

REMARK VARIANT GLUCOCORTICOID RESISTANCE MET-747, AND ALTERED INTERACTION WITH THE COACTIVATOR NCOA2.

COMMENT On or before Mar 15, 2005 this sequence version replaced gi:72116, gi:72117, gi:121070.

[FUNCTION] Receptor for glucocorticoids (GC). Has a dual mode of action: as a transcription factor that binds to glucocorticoid response elements (GRE) and as a modulator of other transcription factors. Affects inflammatory responses, cellular proliferation and differentiation in target tissues.

[SUBUNIT] Heteromultimeric cytoplasmic complex with HSP90, HSP70, and FKBP5 or another immunophilin, or the immunophilin homolog PPP5C. Upon ligand binding FKBP5 dissociates from the complex and FKBP4 takes its place, thereby linking the complex to dynein and mediating transport to the nucleus, where the complex dissociates (By similarity). Binds to DNA as a homodimer, and as a heterodimer with NR3C2 or the retinoid X receptor. Binds STAT5A and STAT5B homodimers and heterodimers. Interacts with NR1P1, POU2F1, POU2F2 and TRIM28 (By similarity). Interacts with several coactivator complexes, including the SMARCA4 complex, CREBBP/EP300, TADA2L and p160 coactivators such as NCOA2 and NCOA6. Interaction with BAG1 inhibits transactivation.

[INTERACTION] P51532:SMARCA4; NbExp=1; IntAct=EBI-493507, EBI-302489; Q92922:SMARCC1; NbExp=1; IntAct=EBI-493507, EBI-355653.

[SUBCELLULAR LOCATION] Cytoplasmic in the absence of ligand; nuclear after ligand-binding.

[ALTERNATIVE PRODUCTS] Event=Alternative splicing; Named isoforms=5; Comment=Additional isoforms seem to exist; Name=Alpha; Synonyms=Alpha-A; IsoId=P04150-1; Sequence=Displayed; Note=Predominant physiological form. Isoform Alpha-B is produced by alternative initiation at Met-27 of isoform Alpha. Both isoforms exhibit similar subcellular location and nuclear translocation after ligand activation. Isoform Alpha-B appears to be more susceptible to degradation, at least when expressed in mammalian cells, but more effective in transcriptional activation and not in transrepression; Name=Beta; Synonyms=Beta-A; IsoId=P04150-2; Sequence=VSP_003703; Note=No hormone-binding activity. Widely expressed at low level. Localized largely in the nucleus. Isoform Beta-B is produced by alternative initiation at Met-27 of isoform Beta; Name=Gamma; Synonyms=Alpha-2, Gamma-A, Alpha-2-A; IsoId=P04150-3; Sequence=VSP_007363; Note=Lower transcriptional activity. Expressed at low level; Name=GR-P; IsoId=P04150-4; Sequence=Not described; Note=Encoded by exons 2-7 plus several basepairs from the subsequent intron region. Lacks the ligand binding domain. Accounts for up to 10-20% of mRNAs; Name=GR-A; IsoId=P04150-5; Sequence=VSP_013340; Note=Lacks exons 5, 6 and 7. Found in glucocorticoid-resistant myeloma patients; Event=Alternative initiation; Comment=At least 4 isoforms, Alpha (shown here), Alpha-B, Beta and Beta-B, are produced by alternative initiation at Met-1 and Met-27. The existence of isoform Alpha and isoform Alpha-B has been proved by mutagenesis. As the sequence environment of the 2 potential ATG initiator codons is the same for the other isoforms, alternative initiation of translation could also occur on these transcripts.

[TISSUE SPECIFICITY] Widely expressed.

[DOMAIN] Composed of three domains: a modulating N-terminal domain, a DNA-binding domain and a C-terminal steroid-binding domain.

[PTM] Increased proteasome-mediated degradation in response to glucocorticoids.

[PTM] Phosphorylated in the absence of hormone; becomes hyperphosphorylated in the presence of glucocorticoid. The

Ser-203-phosphorylated form is mainly cytoplasmic, and the Ser-211-phosphorylated form is nuclear. Transcriptional activity correlates with the amount of phosphorylation at Ser-211.
 [PTM] Sumoylated; this reduces transcription transactivation.
 [DISEASE] Defects in NR3C1 are a cause of glucocorticoid resistance [MIM:138040]; also known as cortisol resistance. It is a hypertensive, hyperandrogenic disorder characterized by increased serum cortisol concentrations. Inheritance is autosomal dominant.
 [SIMILARITY] Belongs to the nuclear hormone receptor family. NR3 subfamily.
 [SIMILARITY] Contains 1 nuclear receptor DNA-binding domain.

FEATURES	Location/Qualifiers
<u>source</u>	1..777 /organism="Homo sapiens" /db_xref="taxon:9606"
<u>gene</u>	1..777 /gene="NR3C1" /note="synonym: GRL"
<u>Protein</u>	1..777 /gene="NR3C1" /product="Glucocorticoid receptor"
<u>Region</u>	1..777 /gene="NR3C1" /region_name="Mature chain" /note="Glucocorticoid receptor, A-type isoforms." /evidence=experimental
<u>Region</u>	1..420 /gene="NR3C1" /region_name="Domain" /note="Modulating." /evidence=experimental
<u>Site</u>	1 /gene="NR3C1" /site_type="mutagenized" /note="M->T: Abolishes expression of A-type isoforms." /evidence=experimental
<u>Region</u>	23 /gene="NR3C1" /region_name="Variant" /note="R -> K (in dbSNP:6190). /FTId=VAR_014140." /evidence=experimental
<u>Region</u>	27..777 /gene="NR3C1" /region_name="Mature chain" /note="Glucocorticoid receptor, B-type isoforms." /evidence=experimental
<u>Site</u>	27 /gene="NR3C1" /site_type="mutagenized" /note="M->T: Abolishes expression of B-type isoforms." /evidence=experimental
<u>Region</u>	29 /gene="NR3C1" /region_name="Variant" /note="F -> L. /FTId=VAR_015628." /evidence=experimental
<u>Region</u>	65 /gene="NR3C1" /region_name="Variant" /note="F -> V (in dbSNP:6192). /FTId=VAR_014622." /evidence=experimental
<u>Region</u>	112 /gene="NR3C1" /region_name="Variant" /note="L -> F. /FTId=VAR_015629." /evidence=experimental
<u>Site</u>	113

Site 141
/gene="NR3C1"
/site_type="modified"
/note="Phosphoserine (By similarity)."
/evidence=not_experimental

Site 191
/gene="NR3C1"
/site_type="modified"
/note="Phosphoserine (By similarity)."
/evidence=not_experimental

Site 193
/gene="NR3C1"
/site_type="mutagenized"
/note="F->D: Reduces transactivation by the ADA complex."
/evidence=experimental

Site 194
/gene="NR3C1"
/site_type="mutagenized"
/note="I->D: Reduces transactivation by the ADA complex."
/evidence=experimental

Site 197
/gene="NR3C1"
/site_type="mutagenized"
/note="L->A: Strongly reduces transactivation by the ADA complex; when associated with V- 224 and F-225."
/evidence=experimental

Site 203
/gene="NR3C1"
/site_type="mutagenized"
/note="L->E: Reduces transactivation by the ADA complex."
/evidence=experimental

Site 211
/gene="NR3C1"
/site_type="modified"
/note="Phosphoserine."
/evidence=experimental

Site 213
/gene="NR3C1"
/site_type="modified"
/note="Phosphoserine."
/evidence=experimental

Site 224
/gene="NR3C1"
/site_type="mutagenized"
/note="W->A: Strongly reduces transactivation by the ADA complex."
/evidence=experimental

Site 225
/gene="NR3C1"
/site_type="mutagenized"
/note="L->V: Strongly reduces transactivation by the ADA complex; when associated with A- 194 and F-225."
/evidence=experimental

Site 226
/gene="NR3C1"
/site_type="mutagenized"
/note="L->F: Strongly reduces transactivation by the ADA complex; when associated with A- 194 and V-224."
/evidence=experimental

Region 233
/gene="NR3C1"
/region_name="Variant"
/note="D -> N. /FTId=VAR_015630."

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/evidence=experimental
Site 235
/gene="NR3C1"
/site_type="mutagenized"
/note="F->L: Strongly reduces transactivation by the ADA
complex; when associated with V- 236."
/evidence=experimental
Site 236
/gene="NR3C1"
/site_type="mutagenized"
/note="L->V: Strongly reduces transactivation by the ADA
complex; when associated with L- 235."
/evidence=experimental
Site 277
/gene="NR3C1"
/site_type="mutagenized"
/note="K->R: Strongly reduces sumoylation. Almost complete
loss of sumoylation; when associated with R-293."
/evidence=experimental
Site 293
/gene="NR3C1"
/site_type="mutagenized"
/note="K->R: Strongly reduces sumoylation. Almost complete
loss of sumoylation; when associated with R-277."
/evidence=experimental
Region 363
/gene="NR3C1"
/region_name="Variant"
/note="N -> S (may increase sensitivity to exogenously
administered glucocorticoids; dbSNP:6195).
/FTId=VAR_004675."
/evidence=experimental
Region 399..418
/gene="NR3C1"
/region_name="Domain"
/note="Glu/Ser/Pro/Thr-rich (PEST region) (Potential).
/evidence=not_experimental
Site 421..486
/gene="NR3C1"
/site_type="DNA binding"
/note="Nuclear receptor-type."
/evidence=experimental
Region 421..441
/gene="NR3C1"
/region_name="Zinc finger region"
/note="C4-type."
/evidence=experimental
Region 421
/gene="NR3C1"
/region_name="Variant"
/note="C -> Y (in a glucocorticoid resistant leukemia cell
line). /FTId=VAR_015631."
/evidence=experimental
Region 451
/gene="NR3C1"
/region_name="Splicing variant"
/note="G -> GR (in isoform Gamma). /FTId=VSP_007363."
/evidence=experimental
Region 457..481
/gene="NR3C1"
/region_name="Zinc finger region"
/note="C4-type."
/evidence=experimental
Region 477
/gene="NR3C1"
/region_name="Variant"
/note="R -> H (in glucocorticoid resistance).

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Region /FTId=VAR_013472."
 /evidence=experimental
 487..527
 /gene="NR3C1"
 /region_name="Domain"
 /note="Hinge."
 /evidence=experimental
Region 491..674
 /gene="NR3C1"
 /region_name="Splicing variant"
 /note="Missing (in isoform GR-A). /FTId=VSP_013340."
 /evidence=experimental
Region 528..777
 /gene="NR3C1"
 /region_name="Domain"
 /note="Steroid-binding."
 /evidence=experimental
Region 559
 /gene="NR3C1"
 /region_name="Variant"
 /note="I -> N (in glucocorticoid resistance; interferes with translocation to the nucleus and thereby strongly reduces transcription activation. Is equally impaired in nuclear export. Acts as dominant negative mutant).
 /FTId=VAR_015632."
 /evidence=experimental
Site 585
 /gene="NR3C1"
 /site_type="mutagenized"
 /note="R->A: Reduces activation mediated by ligand binding domain; when associated with A-590."
 /evidence=experimental
Site 590
 /gene="NR3C1"
 /site_type="mutagenized"
 /note="D->A: Reduces activation mediated by ligand binding domain; when associated with A-585."
 /evidence=experimental
Site 602
 /gene="NR3C1"
 /site_type="mutagenized"
 /note="F->S: Increases solubility. No effect on transactivation by dexamethasone."
 /evidence=experimental
Site 625
 /gene="NR3C1"
 /site_type="mutagenized"
 /note="P->A: Decreases transactivation by dexamethasone by 95%."
 /evidence=experimental
Site 628
 /gene="NR3C1"
 /site_type="mutagenized"
 /note="I->A: Decreases dimerization and transactivation by dexamethasone; when associated with S-602."
 /evidence=experimental
Region 641
 /gene="NR3C1"
 /region_name="Variant"
 /note="D -> V (in glucocorticoid resistance).
 /FTId=VAR_004676."
 /evidence=experimental
Region 679
 /gene="NR3C1"
 /region_name="Variant"
 /note="G -> S (in glucocorticoid resistance; has 50% binding affinity). /FTId=VAR_013473."

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/evidence=experimental
Site 703
/gene="NR3C1"
/site_type="mutagenized"
/note="K->R: Slightly reduces sumoylation."
/evidence=experimental
Region 728..777
/gene="NR3C1"
/region_name="Splicing variant"
/note="VVENLLNYCFQTFLDKTSIEFPEMLAEIITNQIPKYSNGN IKKLLFHQK
-> NVMWLKPESTSHTLI (in isoform Beta). /FTId=VSP_003703."
/evidence=experimental
Region 729
/gene="NR3C1"
/region_name="Variant"
/note="V -> I (in glucocorticoid resistance).
/FTId=VAR_004677."
/evidence=experimental
Region 747
/gene="NR3C1"
/region_name="Variant"
/note="I -> M (in glucocorticoid resistance; alters
interaction with NCOA2 and strongly reduces transcription
activation. Acts as dominant negative mutant).
/FTId=VAR_015633."
/evidence=experimental
Region 753
/gene="NR3C1"
/region_name="Variant"
/note="L -> F (in two glucocorticoid resistant leukemia
cell lines lacking the normal allele). /FTId=VAR_004678."
/evidence=experimental

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ORIGIN

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121 lleesianln rstsvpenpk ssastavsaa ptekefpkth sdvssegqhl kgqgtgtnggn
181 vklytttdqst fdilqdlafs sgspgketne spwrsdllid encllsplug eddsfllegn
241 snedckplil pdkpkikdn gdlvlsspsn vtlpqvktek edfielctpg vikqeklgvt
301 ycqasfpgan iignkmsais vhgvtsggq myhydmtas lsqqqdqkpi fnvippipvg
361 senwnrcqgs gddnltslgt lnfpgrtvfs ngysspsmrp dvssppssss tattgpppk1
421 clvcsdeasg chygvltcgs ckvffkrave gqhnylcagr ndciidkrr kncpacryrk
481 clqagmlea rtkkkkikgi qqattgvsqe tsenpgnkti vpatlpqltp tlvslllevie
541 pevlyagyds svpdstwrin ttlnmlggrq viaavkwaka ipgfrnlhld dqmtllqysw
601 mflmafalgw rsyrqssanl lcfapdliin eqrmtlpcmy dqckhmllys selhrlqvsv
661 eeylcmktll llssvpkdgl ksqelfdeir mtyikelgka ivkregnsq nwqrfyqltk
721 lldsmhevve nllnycfqtfl dktmsiefp emlaeiitnq ipkysngnik kllfhqk

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[\[Sequence\]](#) [\[Tools\]](#)


Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	GCR_HUMAN
Primary accession number	P04150
Secondary accession number	P04151
Entered in Swiss-Prot in	Release 03, November 1986
Sequence was last modified in	Release 03, November 1986
Annotations were last modified in	Release 47, May 2005
Name and origin of the protein	
Protein name	Glucocorticoid receptor
Synonym	GR
Gene name	Name: NR3C1 Synonyms: GRL
From	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.

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"Five missense variants in the amino-terminal domain of the glucocorticoid receptor: no association with puerperal psychosis or schizophrenia.";
Am. J. Med. Genet. 96:412-417(2000).
- [32] VARIANTS GLUCOCORTICOID RESISTANCE HIS-477 AND SER-679.
MEDLINE=21473978;PubMed=11589680 [NCBI, ExPASy, EBI, Israel, Japan]
Ruiz M., Lind U., Gaafvels M., Eggertsen G., Carlstedt-Duke J., Nilsson L., Holtmann M., Stierna P., Wikstroem A.-C., Werner S.;
"Characterization of two novel mutations in the glucocorticoid receptor gene in patients with primary cortisol resistance.";
Clin. Endocrinol. (Oxf.) 55:363-371(2001).
- [33] CHARACTERIZATION OF VARIANT GLUCOCORTICOID RESISTANCE ASN-559.
DOI=10.1210/jc.86.11.5600;MEDLINE=21558592;PubMed=11701741 [NCBI, ExPASy, EBI, Israel, Japan]

Kino T., Stauber R.H., Resau J.H., Pavlakis G.N., Chrousos G.P.;

"Pathologic human GR mutant has a transdominant negative effect on the wild-type GR by inhibiting its translocation into the nucleus: importance of the ligand-binding domain for intracellular GR trafficking.";

J. Clin. Endocrinol. Metab. 86:5600-5608(2001).

[34] VARIANT GLUCOCORTICOID RESISTANCE MET-747, AND ALTERED INTERACTION WITH THE COACTIVATOR NCOA2.

DOI=10.1210/jc.87.6.2658;MEDLINE=22045363;PubMed=12050230 [NCBI, ExPASy, EBI, Israel, Japan]

Vottero A., Kino T., Combe H., Lecomte P., Chrousos G.P.;

"A novel, C-terminal dominant negative mutation of the GR causes familial glucocorticoid resistance through abnormal interactions with p160 steroid receptor coactivators.";

J. Clin. Endocrinol. Metab. 87:2658-2667(2002).

Comments

- **FUNCTION:** Receptor for glucocorticoids (GC). Has a dual mode of action: as a transcription factor that binds to glucocorticoid response elements (GRE) and as a modulator of other transcription factors. Affects inflammatory responses, cellular proliferation and differentiation in target tissues.
- **SUBUNIT:** Heteromultimeric cytoplasmic complex with HSP90, HSP70, and FKBP5 or another immunophilin, or the immunophilin homolog PPP5C. Upon ligand binding FKBP5 dissociates from the complex and FKBP4 takes its place, thereby linking the complex to dynein and mediating transport to the nucleus, where the complex dissociates (*By similarity*). Binds to DNA as a homodimer, and as a heterodimer with NR3C2 or the retinoid X receptor. Binds STAT5A and STAT5B homodimers and heterodimers. Interacts with NR1P1, POU2F1, POU2F2 and TRIM28 (*By similarity*). Interacts with several coactivator complexes, including the SMARCA4 complex, CREBBP/EP300, TADA2L and p160 coactivators such as NCOA2 and NCOA6. Interaction with BAG1 inhibits transactivation.
- **SUBCELLULAR LOCATION:** Cytoplasmic in the absence of ligand; nuclear after ligand-binding.
- **ALTERNATIVE PRODUCTS:**

Alternative splicing [5 named forms]

Alternative initiation

Comment: Additional isoforms seem to exist.

Name **Alpha**

Synonyms Alpha-A

Isoform ID P04150-1

Note: Predominant physiological form. Isoform Alpha-B is produced by alternative initiation at Met-27 of isoform Alpha. Both isoforms exhibit similar subcellular location and nuclear translocation after ligand activation. Isoform Alpha-B appears to be more susceptible to degradation, at least when expressed in mammalian cells, but more effective in transcriptional activation and not in transrepression.

This is the isoform sequence displayed in this entry.

Name **Beta**

Synonyms Beta-A

Isoform ID P04150-2

Note: No hormone-binding activity. Widely expressed at low level. Localized largely in the nucleus. Isoform Beta-B is produced by alternative initiation at Met-27 of isoform Beta.

Features which should be applied to build the isoform sequence: VSP_003703.

Name Gamma

Synonyms Alpha-2, Gamma-A, Alpha-2-A

Isoform ID P04150-3

Note: Lower transcriptional activity. Expressed at low level.

Features which should be applied to build the isoform sequence: VSP_007363.

Name GR-P

Isoform ID P04150-4

Note: Encoded by exons 2-7 plus several basepairs from the subsequent intron region.

Lacks the ligand binding domain. Accounts for up to 10-20% of mRNAs.

The sequence of this isoform is not described.

Name GR-A

Isoform ID P04150-5

Note: Lacks exons 5, 6 and 7. Found in glucocorticoid-resistant myeloma patients.

Features which should be applied to build the isoform sequence: VSP_013340.

Comment: At least 4 isoforms, Alpha (shown here), Alpha-B, Beta and Beta-B, are produced by alternative initiation at Met-1 and Met-27. The existence of isoform Alpha and isoform Alpha-B has been proved by mutagenesis. As the sequence environment of the 2 potential ATG initiator codons is the same for the other isoforms, alternative initiation of translation could also occur on these transcripts.

- **TISSUE SPECIFICITY:** Widely expressed.
- **DOMAIN:** Composed of three domains: a modulating N-terminal domain, a DNA-binding domain and a C-terminal steroid-binding domain.
- **PTM:** Increased proteasome-mediated degradation in response to glucocorticoids.
- **PTM:** Phosphorylated in the absence of hormone; becomes hyperphosphorylated in the presence of glucocorticoid. The Ser-203-phosphorylated form is mainly cytoplasmic, and the Ser-211-phosphorylated form is nuclear. Transcriptional activity correlates with the amount of phosphorylation at Ser-211.
- **PTM:** Sumoylated; this reduces transcription transactivation.
- **DISEASE:** Defects in NR3C1 are a cause of glucocorticoid resistance [MIM:138040]; also known as cortisol resistance. It is a hypertensive, hyperandrogenic disorder characterized by increased serum cortisol concentrations. Inheritance is autosomal dominant.
- **SIMILARITY:** Belongs to the nuclear hormone receptor family. NR3 subfamily.
- **SIMILARITY:** Contains 1 nuclear receptor DNA-binding domain.

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Cross-references

X03225; CAA26976.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
X03348; CAA27054.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
U80946; AAB64353.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
U78506; AAB64353.1; JOINED.[EMBL / GenBank / DDBJ] [CoDingSequence]
U78507; AAB64353.1; JOINED.[EMBL / GenBank / DDBJ] [CoDingSequence]
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	U01351; AAA16603.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AY436590; AAQ97180.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	BC015610; AAH15610.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	M69104; AAA88049.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	M73816; AAA53151.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	S68378; AAB20466.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AC005601; AAC34207.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
PDB	A93370; QRHUGA.
	B93370; QRHUGB.
	1M2Z; X-ray; A/D=521-777. [ExPASy / RCSB / EBI]
	1NHZ; X-ray; A=500-777. [ExPASy / RCSB / EBI]
SMR	1P93; X-ray; A/B/C/D=500-777.[ExPASy / RCSB / EBI]
	Detailed list of linked structures.
IntAct	P04150; 417-491.
TRANSFAC	P04150; -.
	T00337; -.
Ensembl	T01920; -.
Genew	ENSG00000113580; Homo sapiens. [Contig view]
CleanEx	HGNC:7978; NR3C1.
GeneCards	HGNC:7978; NR3C1.
GeneLynx	NR3C1.
GenAtlas	NR3C1; Homo sapiens.
NIEHS-SNPs	NR3C1.
H-InvDB	NR3C1.
MIM	HIX0005273; -.
GO	138040 [NCBI / EBI].
	GO:0005737; Cellular component: cytoplasm (<i>traceable author statement</i>).
	GO:0005759; Cellular component: mitochondrial matrix (<i>traceable author statement</i>).
	GO:0005634; Cellular component: nucleus (<i>traceable author statement</i>).
	GO:0004883; Molecular function: glucocorticoid receptor activity (<i>traceable author statement</i>).
	GO:0003700; Molecular function: transcription factor activity (<i>traceable author statement</i>).
	GO:0007165; Biological process: signal transduction (<i>traceable author statement</i>).
	GO:0006366; Biological process: transcription from Pol II promoter (<i>traceable author statement</i>).

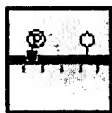
QuickGo
view:

SOURCE NR3C1; Homo sapiens.
IPR001409; Glcrtcd_receptor.
IPR000536; Hrmon_recept_lig.
InterPro IPR001723; Stdhrmn_receptor.
IPR008946; Str_ncl_receptor.
IPR001628; Znf_C4steroid.
Graphical view of domain structure.
PF02155; GCR; 1.
Pfam PF00104; Hormone_recep; 1.
PF00105; zf-C4; 1.
Pfam graphical view of domain structure.
PRINTS PR00528; GLCORTICOIDR.
PR00398; STRDHORMONER.
PR00047; STROIDFINGER.
ProDom PD000035; Znf_C4steroid; 1.
[Domain structure / List of seq. sharing at least 1 domain]
SMART SM00430; HOLI; 1.
SM00399; ZnF_C4; 1.
PROSITE PS00031; NUCLEAR_REC_DBD_1; 1.
PS51030; NUCLEAR_REC_DBD_2; 1.
PROSITE graphical view of domain structure.
NucleaRDB P04150; GCR_HUMAN.
HOVERGEN [Family / Alignment / Tree]
BLOCKS P04150.
ProtoNet P04150.
ProtoMap P04150.
PRESAGE P04150.
DIP P04150.
ModBase P04150.
SWISS-2DPAGE Get region on 2D PAGE.
UniRef View cluster of proteins with at least 50% / 90% identity.

Keywords

3D-structure; Alternative initiation; Alternative splicing; Disease mutation; DNA-binding; Nuclear protein; Phosphorylation; Polymorphism; Receptor; Steroid-binding; Trans-acting factor; Transcription; Transcription regulation; Ubl conjugation; Zinc-finger.

Features



Feature table viewer



Feature aligner

Key	From	To	Length	Description	FTId
CHAIN	1	777	777	Glucocorticoid receptor, A-type isoforms.	
CHAIN	27	777	751	Glucocorticoid receptor, B-type isoforms.	
INIT_MET	27	27		For B-type isoforms.	

DOMAIN	1	420	420	Modulating.	
DOMAIN	399	418	20	Glu/Ser/Pro/Thr-rich (PEST region) (Potential).	
DNA_BIND	421	486	66	Nuclear receptor-type.	
ZN_FING	421	441	21	C4-type.	
ZN_FING	457	481	25	C4-type.	
DOMAIN	487	527	41	Hinge.	
DOMAIN	528	777	250	Steroid-binding.	
MOD_RES	113	113		Phosphoserine (By similarity).	
MOD_RES	141	141		Phosphoserine (By similarity).	
MOD_RES	203	203		Phosphoserine.	
MOD_RES	211	211		Phosphoserine.	
MOD_RES	226	226		Phosphoserine (By similarity).	
VARSP LIC	728	777		VVENLLNYCFQTFLDKTMSIEFPEMLAEIITNQIPKYSNG NIKKLLFHQK -> NVMWLKPESTSHTLI (in isoform Beta).	VSP_003703
VARSP LIC	451	451		G -> GR (in isoform Gamma).	VSP_007363
VARSP LIC	491	674		Missing (in isoform GR-A).	VSP_013340
VARIANT	23	23	1	R -> K (in dbSNP:6190) [NCBI/Ensembl].	VAR_014140
VARIANT	29	29	1	F -> L.	VAR_015628
VARIANT	65	65	1	F -> V (in dbSNP:6192) [NCBI/Ensembl].	VAR_014622
VARIANT	112	112	1	L -> F.	VAR_015629
VARIANT	233	233	1	D -> N.	VAR_015630
VARIANT	363	363	1	N -> S (may increase sensitivity to exogenously administered glucocorticoids; dbSNP:6195) [NCBI/Ensembl].	VAR_004675
VARIANT	421	421	1	C -> Y (in a glucocorticoid resistant leukemia cell line).	VAR_015631
VARIANT	477	477	1	R -> H (in glucocorticoid resistance).	VAR_013472
VARIANT	559	559	1	I -> N (in glucocorticoid resistance; interferes with translocation to the nucleus and thereby strongly reduces transcription activation. Is equally impaired in nuclear export. Acts as dominant negative mutant).	VAR_015632 [3D]
VARIANT	641	641	1	D -> V (in glucocorticoid resistance).	VAR_004676 [3D]
VARIANT	679	679	1	G -> S (in glucocorticoid resistance; has 50% binding affinity).	VAR_013473 [3D]
VARIANT	729	729	1	V -> I (in glucocorticoid resistance).	VAR_004677 [3D]
VARIANT	747	747	1	I -> M (in glucocorticoid resistance; alters interaction with NCOA2 and strongly reduces transcription activation. Acts as dominant negative mutant).	VAR_015633 [3D]
VARIANT	753	753	1	L -> F (in two glucocorticoid resistant leukemia cell lines lacking the normal allele).	VAR_004678 [3D]
MUTAGEN	1	1		M->T: Abolishes expression of A-type isoforms.	
MUTAGEN	27	27		M->T: Abolishes expression of B-type isoforms.	
MUTAGEN	191	191		F->D: Reduces transactivation by the ADA complex.	
MUTAGEN	193	193		I->D: Reduces transactivation by the ADA	

MUTAGEN	194	194	complex. L->A: Strongly reduces transactivation by the ADA complex; when associated with V-224 and F-225.
MUTAGEN	197	197	L->E: Reduces transactivation by the ADA complex.
MUTAGEN	213	213	W->A: Strongly reduces transactivation by the ADA complex.
MUTAGEN	224	224	L->V: Strongly reduces transactivation by the ADA complex; when associated with A-194 and F-225.
MUTAGEN	225	225	L->F: Strongly reduces transactivation by the ADA complex; when associated with A-194 and V-224.
MUTAGEN	235	235	F->L: Strongly reduces transactivation by the ADA complex; when associated with V-236.
MUTAGEN	236	236	L->V: Strongly reduces transactivation by the ADA complex; when associated with L-235.
MUTAGEN	277	277	K->R: Strongly reduces sumoylation. Almost complete loss of sumoylation; when associated with R-293.
MUTAGEN	293	293	K->R: Strongly reduces sumoylation. Almost complete loss of sumoylation; when associated with R-277.
MUTAGEN	585	585	R->A: Reduces activation mediated by ligand binding domain; when associated with A-590.
MUTAGEN	590	590	D->A: Reduces activation mediated by ligand binding domain; when associated with A-585.
MUTAGEN	602	602	F->S: Increases solubility. No effect on transactivation by dexamethasone.
MUTAGEN	625	625	P->A: Decreases transactivation by dexamethasone by 95%.
MUTAGEN	628	628	I->A: Decreases dimerization and transactivation by dexamethasone; when associated with S-602.
MUTAGEN	703	703	K->R: Slightly reduces sumoylation.

Sequence information

Length: **777 AA** [This is the length of the unprocessed precursor]

Molecular weight: **85659 Da** [This is the MW of the unprocessed precursor]

CRC64: **C5C90C9A5DD16AAB** [This is a checksum on the sequence]

10	20	30	40	50	60
MDSKESLTPG	REENPSSVLA	QERGDVMDFY	KTLRGGATVK	VSASSPSLAV	ASQSDSKQRR
70	80	90	100	110	120
LLVDFPKGSV	SNAQQPDL SK	AVSLSMGLYM	GETETKVMGN	DLGFPQQGQI	SLSSGETDLK
130	140	150	160	170	180
LLEESIANLN	RSTSVPENPK	SSASTAVSAA	PTEKEFPKTH	SDVSSEQQHL	KGQTGTNGGN
190	200	210	220	230	240
VKLYTTDQST	FDILQDLEFS	SGSPGKETNE	SPWRSDLLID	ENCLISPLAG	EDDSFLLEGN
250	260	270	280	290	300


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SNEDCKPLIL PDKPKIKDN GDLVLSSPSN VTLPQVKTEK EDFIELCTPG VIKQEKLGTV
      310      320      330      340      350      360
YCQASFPGAN IIGNKMSAIS VHGVSTSGGQ MYHYDMNTAS LSQQQDQKPI FNVIPPIPVG

      370      380      390      400      410      420
SENWNRQGS GDDNLTSLGT LNFPGRTVFS NGYSSPSMRP DVSSPPSSSS TATTGPPPKL

      430      440      450      460      470      480
CLVCSDEASG CHYGVLTCGS CKVFFKRAVE GQHNYLCAGR NDCIIDKIRR KNCPACRYRK

      490      500      510      520      530      540
CLQAGMNLEA RKTKKKIKGI QQATTGVSQE TSENPKNKTI VPATLPQLTP TLVSLLEVIE

      550      560      570      580      590      600
PEVLYAGYDS SVPDSTWRIM TTLNMLGGRQ VIAAVKWAKA IPGFRNLHLD DQMTLLQYSW

      610      620      630      640      650      660
MFLMAFALGW RSYRQSSANL LCFAPDLIIN EQRM TLPCMY DQCKHMLYVS SELHRLQVSY

      670      680      690      700      710      720
EEYLCMKTLL LLSSVPKDGL KSQELFDEIR MTYIKELGKA IVKREGNSSQ NWQRFYQLTK

      730      740      750      760      770
LLDSMHEVVE NLLNYCFQTF LDKTMSIEFP EMLAEIITNQ IPKYSNGNIK KLLFHQK

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Compute pI/Mw, PeptideMass, PeptideCutter,
Dotlet (Java)



ScanProsite, MotifScan



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